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APPLICATION NO.	FILING DATE	FIRST NAMED INVENTOR	ATTORNEY DOCKET NO.	CONFIRMATION NO.
10/654,365	09/03/2003	Chris Rundfeldt	NY-HUBR-1250-US	4231

24972 7590 06/12/2006

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EXAMINER	
ISSAC, ROY P	

ART UNIT	PAPER NUMBER
1623	

DATE MAILED: 06/12/2006

Please find below and/or attached an Office communication concerning this application or proceeding.

Office Action Summary	Application No.	Applicant(s)	
	10/654,365	RUNDFELDT ET AL.	
	Examiner	Art Unit	
	Roy P. Issac	1623	

-- The MAILING DATE of this communication appears on the cover sheet with the correspondence address --

Period for Reply

A SHORTENED STATUTORY PERIOD FOR REPLY IS SET TO EXPIRE 3 MONTH(S) OR THIRTY (30) DAYS, WHICHEVER IS LONGER, FROM THE MAILING DATE OF THIS COMMUNICATION.

- Extensions of time may be available under the provisions of 37 CFR 1.136(a). In no event, however, may a reply be timely filed after SIX (6) MONTHS from the mailing date of this communication.
- If NO period for reply is specified above, the maximum statutory period will apply and will expire SIX (6) MONTHS from the mailing date of this communication.
- Failure to reply within the set or extended period for reply will, by statute, cause the application to become ABANDONED (35 U.S.C. § 133). Any reply received by the Office later than three months after the mailing date of this communication, even if timely filed, may reduce any earned patent term adjustment. See 37 CFR 1.704(b).

Status

1)☐ Responsive to communication(s) filed on _____.

2a)☐ This action is **FINAL**. 2b)☒ This action is non-final.

3)☐ Since this application is in condition for allowance except for formal matters, prosecution as to the merits is closed in accordance with the practice under *Ex parte Quayle*, 1935 C.D. 11, 453 O.G. 213.

Disposition of Claims

4)☒ Claim(s) *1-4* is/are pending in the application.

4a) Of the above claim(s) _____ is/are withdrawn from consideration.

5)☐ Claim(s) _____ is/are allowed.

6)☒ Claim(s) *1-4* is/are rejected.

7)☐ Claim(s) _____ is/are objected to.

8)☐ Claim(s) _____ are subject to restriction and/or election requirement.

Application Papers

9)☐ The specification is objected to by the Examiner.

10)☐ The drawing(s) filed on _____ is/are: a)☐ accepted or b)☐ objected to by the Examiner.

Applicant may not request that any objection to the drawing(s) be held in abeyance. See 37 CFR 1.85(a).

Replacement drawing sheet(s) including the correction is required if the drawing(s) is objected to. See 37 CFR 1.121(d).

11)☐ The oath or declaration is objected to by the Examiner. Note the attached Office Action or form PTO-152.

Priority under 35 U.S.C. § 119

12)☒ Acknowledgment is made of a claim for foreign priority under 35 U.S.C. § 119(a)-(d) or (f).

a)☐ All b)☐ Some * c)☐ None of:

1.☒ Certified copies of the priority documents have been received.

2.☐ Certified copies of the priority documents have been received in Application No. _____.

3.☐ Copies of the certified copies of the priority documents have been received in this National Stage application from the International Bureau (PCT Rule 17.2(a)).

* See the attached detailed Office action for a list of the certified copies not received.

Attachment(s)

1) ☒ Notice of References Cited (PTO-892)
2) ☐ Notice of Draftsperson's Patent Drawing Review (PTO-948)
3) ☒ Information Disclosure Statement(s) (PTO-1449 or PTO/SB/08) Paper No(s)/Mail Date *3/19/04*.
4) ☐ Interview Summary (PTO-413) Paper No(s)/Mail Date. _____.
5) ☐ Notice of Informal Patent Application (PTO-152)
6) ☐ Other: _____.

DETAILED ACTION

Status of the Application

This application claims the benefit for foreign priority to German application 102 41 407.6, filed on September 06, 2002 under 35 U.S.C 119(a)-(d). The copy of certified copy of the priority has been filed with the instant Application. It is noted that Germany 102 41 407.6 is in German; no translation of said Germany application into English has been provided.

Claims 1-4 are currently pending and are examined on the merits.

Double Patenting

The nonstatutory double patenting rejection is based on a judicially created doctrine grounded in public policy (a policy reflected in the statute) so as to prevent the unjustified or improper timewise extension of the "right to exclude" granted by a patent and to prevent possible harassment by multiple assignees. A nonstatutory obviousness-type double patenting rejection is appropriate where the conflicting claims are not identical, but at least one examined application claim is not patentably distinct from the reference claim(s) because the examined application claim is either anticipated by, or would have been obvious over, the reference claim(s). See, e.g., *In re Berg*, 140 F.3d 1428, 46 USPQ2d 1226 (Fed. Cir. 1998); *In re Goodman*, 11 F.3d 1046, 29 USPQ2d 2010 (Fed. Cir. 1993); *In re Longi*, 759 F.2d 887, 225 USPQ 645 (Fed. Cir. 1985); *In re Van Ornum*, 686 F.2d 937, 214 USPQ 761 (CCPA 1982); *In re Vogel*, 422 F.2d 438, 164 USPQ 619 (CCPA 1970); and *In re Thorington*, 418 F.2d 528, 163 USPQ 644 (CCPA 1969).

A timely filed terminal disclaimer in compliance with 37 CFR 1.321(c) or 1.321(d) may be used to overcome an actual or provisional rejection based on a nonstatutory double patenting ground provided the conflicting application or patent either is shown to be commonly owned with this application, or claims an invention made as a result of activities undertaken within the scope of a joint research agreement.

Effective January 1, 1994, a registered attorney or agent of record may sign a terminal disclaimer. A terminal disclaimer signed by the assignee must fully comply with 37 CFR 3.73(b).

Claims 1, 3 and 4 are rejected on the ground of nonstatutory obviousness-type double patenting as being unpatentable over claims 19-22 of U.S. Patent No. 6,613,794 by Hofgen et. al. (PTO-1449, Included by the applicant), in view of Kaliner et. al. (PTO-892, Cited by the examiner).

Although the conflicting claims are not identical, they are not patentably distinct from each other because the patent is drawn to a method of inhibiting phosphodiesterase 4 (PDE4) and tumour necrosis factor α (TNFα) release by the use of hydroxyindols.

The claims of the instant application are drawn to the treatment of nonallergic rhinitis by the use of compounds of the general formula I. Note that some of the compounds of the general formula I, and the hydroxyindols disclosed in Hofgen are the same.

The '794 patent does not expressly disclose the treatment of nonallergic rhinitis by hydroxyindols, or the use of the same for the treatment of nonallergic rhinitis caused by bacterial, viral or fungal infection.

Claims 19-22 in Hofgen et. al., U.S. Patent # 6,613,794, are directed to the use of hydroxyindols for the inhibition of TNFα and PDE4. (Column 18, lines 54-68). Hofgen et. al, discloses that "An important property of phospodiesterase 4 inhibitors is the inhibition of the release of tumour necrosis factor α (TNFα) from inflammatory cells." (Column 1, lines 52-56). Hofgen et. al. further discloses that "Inhibitors of phosphodiesterase 4 are thus also suitable for the therapy of disorders of this type which are associated with TNFα." (Column 2, lines 7-10).

Kaliner et. al, discloses that release of TNFα is known to be associated with chronic sinusitis, which is one of the nonallergic rhinitis diseases listed in claim 3 of the instant application. (Page S832, Column 2, Paragraph 2, lines 11-15). Kaliner et. al. further teaches that acute sinusitis is caused by viral and bacterial infections. (Page S830, Column 1, Paragraph 2, lines 3-10).

One having ordinary skill in the art would have been motivated to use compounds of formula 1 to treat nonallergic rhinitis because compounds of formula I were well known for inhibition of PDE4 and TNFα release, and nonallergic rhinitis is known to be associated with TNFα. Therefore, one of ordinary skill in the art would have reasonably expected that the use of compounds of formula I would be effective for the treatment of nonallergic rhinitis.

Claims 1-4 are rejected on the ground of nonstatutory obviousness-type double patenting as being unpatentable over claims 5-8 of U.S. Patent No. 6,251,923 by Hofgen et. al. (PTO-1449, Included by the applicant), in view of Kaliner et. al. (PTO-892, Cited by the examiner).

Although the conflicting claims are not identical, they are not patentably distinct from each other because the patent is drawn to a method of inhibiting phosphodiesterase 4 (PDE4) and tumour necrosis factor α (TNFα) release by the use of hydroxyindols.

The claims of the instant application are drawn to the treatment of nonallergic rhinitis by the use of compounds of the general formula I. Note that some of the compounds of the general formula I, and the hydroxyindols disclosed in Hofgen are the same.

The '923 patent does not expressly disclose the treatment of nonallergic rhinitis by hydroxyindols, or the use of the same for the treatment of nonallergic rhinitis caused by bacterial, viral or fungal infection.

Claims 5-8 in Hofgen, U.S. Patent # 6,251,923, are directed to the use of hydroxyindols for the inhibition of TNFα and PDE4. (Column 18, lines 31-43). Some of the compounds of general formula I are structurally identical to the disclosed hydroxyindols in '923 patent. Hofgen et. al, teaches the role of PDE4 inhibitors in inhibiting the release of TNFα. (Column 1, Paragraph 4, lines 50-67 and Column 2, lines 1-4). Hofgen et. al. discloses that "An important property of phospodiesterase 4 inhibitors is the inhibition of the release of tumour necrosis factor α (TNFα) from inflammatory cells." (Column 1, lines 50-54). Hofgen et. al. further discloses that "Inhibitors of phosphodiesterase 4 are thus also suitable for the therapy of disorders of this type which are associated with TNFα." (Column 2, lines 1-3).

As discussed above, Kaliner et. al, discloses that release of TNFα is known to be associated with chronic sinusitis, which is one of the nonallergic rhinitis diseases listed in claim 3 of the instant application. (Page S832, Column 2, Paragraph 2, lines 11-15). Kaliner et. al. further teaches that acute sinusitis is caused by viral and bacterial infections. (Page S830, Column 1, Paragraph 2, lines 3-10).

One having ordinary skill in the art would have been motivated to use compounds of formula 1 to treat nonallergic rhinitis because compounds of formula I were well known for inhibition of PDE4 and TNFα release, and nonallergic rhinitis is known to be associated with TNFα. Therefore, one of ordinary skill in the art would have reasonably expected that the use of compounds of formula I would be effective for the treatment of nonallergic rhinitis.

Claim Rejections - 35 USC § 103

The following is a quotation of 35 U.S.C. 103(a) which forms the basis for all obviousness rejections set forth in this Office action:

> (a) A patent may not be obtained though the invention is not identically disclosed or described as set forth in section 102 of this title, if the differences between the subject matter sought to be patented and the prior art are such that the subject matter as a whole would have been obvious at the time the invention was made to a person having ordinary skill in the art to which said subject matter pertains. Patentability shall not be negatived by the manner in which the invention was made.

Claims 1-3 are rejected under 35 U.S.C. 103(a) as being unpatentable over Richter et. al. (PTO-892, cited by the examiner) in view of Azria et. al. (U.S. Patent # 5,561,149, PTO-1449, Included by the applicant).

Richter et. al. teach the use of PDE4 inhibitors, in particular, AWD 12-281, for the treatment of asthma. (Page 287, Abstract, lines 12-17 and Page 288, Column 1, lines 4-9 and Page 290 Figure 1).

Richter does not expressly teach the use of PDE4 inhibitors for the treatment of nonallergic rhinitis.

Azria discloses the use of a group of imidazolyl carbazols for the treatment of rhinitis. (Abstract, lines 3-5, and Column 1, lines 50-55). Azria et. al. teaches the use of imidazolyl carbozols for the treatment of stress-related rhinitis. (Column 1, lines 48-53). Specification of the present application defines "nonallergic rhinitis" as a whole series of disorders which involve the symptoms of chronic rhinitis but which do not have an allergic origin." (Specification, Page 1, lines 10-15). Note that some of the compounds of formula I in the instant application are encompassed by the generic formula I-II in the '149 patent. (Columns 2-4). For example, a compound where;

A = II, where R_1 is hydroxyl; R_2 is a C1 alkoxy; and Z is NR_3;

B = -CO-

C = NH, and

D = any one of the disclosed heterocycles with N as the heteroatom,

will read on one or more of the compounds disclosed in the current application.

It would have been obvious to a person of ordinary skill in the art at the time the invention was made to employ the compounds of formula I, in particular AWD 12-281, for the treatment of nonallergic rhinitis.

One having ordinary skill in the art at the time the invention was made would have been motivated to use compounds of formula I, because AWD 12-281, one of the compounds of general formula I, is known in the prior art and compounds of formula I are broadly covered and encompassed in the '149 patent for the treatment of nonallergic rhinitis.

Therefore, one of ordinary skill in the art would have reasonably expected that the instant compounds of formula I, in particular AWD 12-281 would have the same or substantially similar beneficial therapeutic effects and usefulness for treating nonallergic rhinitis. If the claimed invention and the structurally similar prior art species share any useful property, that will generally be sufficient to motivate an artisan of ordinary skill to make the claimed species. It is a reasonable expectation that similar species usually have similar properties. See Dillon, 919 F.2d at 693, 696, 16 USPQ2d at 1901, 1904. See also, Deuel, 51 F.3d at 1558, 34 USPQ2d at 1214. In fact, similar properties may

formally be presumed when compounds are very close in structure. Dillon 919 F.2d at 693, 696, 16 USPQ2d at 1901, 1904, as noted in MPEP 2144.

Claims 1-4 are rejected under 35 U.S.C. 103(a) as being unpatentable over Hofgen et. al, (U.S. Patent # 6,251,923 or U.S. Patent # 6,613,794, PTO-1449, Included by the applicant), in view of Kaliner et. al. (PTO-892, Cited by the examiner).

Hofgen et. al. teaches the use of hydroxyindols for the inhibition of phosphodiesterase 4 (PDE4). (Column 1, lines 5-14). Note that hydroxyindoles of Hofgen reference has the same structure as the compounds of the present application and thus are the same. Hofgen et. al, further teaches the role of PDE4 inhibitors in inhibiting the release of TNFα. (Column 1, Paragraph 4, lines 50-67 and Column 2, lines 1-4). The author notes that "An important property of phospodiesterase 4 inhibitors is the inhibition of the release of tumour necrosis factor α (TNFα) from inflammatory cells." (Column 1, lines 50-54). Hofgen et. al. further discloses that "Inhibitors of phosphodiesterase 4 are thus also suitable for the therapy of disorders of this type which are associated with TNFα." (Column 2, lines 1-3). Hofgen et. al, further teaches the use of hydroxyindoles for inhibiting TNFα release and phosphodiesterase 4. (Claims 5-8, Column 18, lines 31-43).

Hofgen does not expressly disclose the use of hydroxyindoles for the treatment of the class of diseases considered as nonallergic rhinitis. Hofgen doesn't disclose the treatment of nonallergic rhinitis caused by bacterial, viral or fungal infection.

Kaliner et. al, teaches that release of TNFα is associated with chronic sinusitis, one of the nonallergic rhinitis diseases listed in claim 3. (Page S832, Column 2, Paragraph 2, lines 11-15). Kaliner et. al. further disclose that acute sinusitis is caused by viral and bacterial infections. (Page S830, Column 1, Paragraph 2, lines 3-10).

It would have been obvious to one of ordinary skill in the art at the time the invention was made to treat nonallergic rhinitis with a compound of formula I, because compounds of formula I were well known for their effectiveness in PDE4 inhibtion and TNFα release was known to be associated with nonallergic rhinitis and PDE4 is known to play an important role in TNFα release.

One having ordinary skill in the art would have been motivated to use compounds of formula 1 to treat nonallergic rhinitis because compounds of formula I were well known for inhibition of PDE4 and TNFα release, and nonallergic rhinitis is known to be associated with TNFα.

Therefore, one of ordinary skill in the art would have reasonably expected that the use of compounds of formula I would be effective against nonallergic rhinitis. Thus the claimed invention as a whole is clearly prima facie obvious over the combined teachings of the prior art.

Claims 1-3 are rejected under 35 U.S.C. 103(a) as being unpatentable over Locher et. al, in view of Locher et. al, (U.S. Patent Publication # 2005/0288265 A1,

PTO-892 Cited by the examiner) in view of Ignacio J, et. al. (PTO-892, Cited by the examiner).

Locher et. al, discloses that the use of hydroxyindols, in particular, N-(3,5-di-chloropyridin-4-yl)-2-[1-(4-fluorobenzyl)-5-hydroxyindol-3-yl]-oxoacetamide, is effective as a PDE4 inhibitor and in the treatment of respiratory diseases. (Column 1, Paragraph 1, lines 3-10).

Locher does not expressly disclose the use of hydroxyindols for the treatment of nonallergic rhinitis or the use of hydroxyindols for treatment against nonallergic rhinitis caused by virus, bacteria or fungus.

Ignacio et. al, discloses that respiratory diseases include chronic sinusitis, one of the nonallergic rhinitis listed in claim 3 herein. (Page 65, Paragraph 4, lines 1-5) Ignacio et. al further shows that other respiratory diseases can also result from bacterial and viral infections. (Page 65, Paragraph 2, lines 4-10 and Paragraph 4, lines 1-5).

It would have been obvious to a person of ordinary skill in the art at the time the invention was made to use compounds of formula I, in particular N-(3,5-di-chloropyridin-4-yl)-2-[1-(4-fluorobenzyl)-5-hydroxyindol-3-yl]-oxoacetamide to treat chronic sinusitis, a nonallergic rhinitis disease, because chronic sinusitis is a respiratory disease and compounds of formula I are known to be effective against respiratory diseases.

One having ordinary skill in the art would have been motivated to use compounds of formula 1 to treat nonallergic rhinitis because compounds of formula I were well known for the treatment of respiratory diseases and chronic sinusitis, a nonallergic rhinitis disease, is also well known as a respiratory disease.

Therefore, one of ordinary skill in the art would have reasonably expected that the use of compounds of formula I would be effective against nonallergic rhinitis. Thus, the claimed invention as a whole is clearly prima facie obvious over the combined teachings of the prior art.

Any inquiry concerning this communication or earlier communications from the examiner should be directed to Roy P. Issac whose telephone number is 571-272-2674. The examiner can normally be reached on 9:00-5:00.

If attempts to reach the examiner by telephone are unsuccessful, the examiner's supervisor, Shaojia Anna Jiang can be reached on 571-272-0627. The fax phone number for the organization where this application or proceeding is assigned is 571-273-8300.

Information regarding the status of an application may be obtained from the Patent Application Information Retrieval (PAIR) system. Status information for published applications may be obtained from either Private PAIR or Public PAIR. Status information for unpublished applications is available through Private PAIR only. For more information about the PAIR system, see http://pair-direct.uspto.gov. Should you have questions on access to the Private PAIR system, contact the Electronic Business Center (EBC) at 866-217-9197 (toll-free). If you would like assistance from a USPTO Customer Service Representative or access to the automated information system, call 800-786-9199 (IN USA OR CANADA) or 571-272-1000.

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April 28, 2006

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